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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,676	06/08/2000	ANDREA CRISANTI	GJE-39	9050

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GAINESVILLE, FL 32606-6669

EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 10/23/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/486,676

Applicant(s)

CRISANTI, ANDREA

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 16, 17 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 8, 9, 19 and 21 is/are rejected.
- 7) ☐ Claim(s) 4-7, 20, 22 and 23 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

Claims 1-14, 16, 17 and 19-24 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the special technical features that link the claims in the subject application define a contribution which each of the claims makes over the prior art. Applicant asserts that the Schutze-Redelmeier reference does not disclose conjugates of antennapedia that have a second region with greater than 100 amino acids as recited in claim 4. Applicant further asserts that the Schutze-Redelmeier reference teaches that the purification process of the conjugates involves a high salt KCl, hence the product is not in non-denaturing conditions. Applicants further argue that the PCT application corresponding to the current application was determined to have unity of invention among all claims; and the International Preliminary Examination Report indicated that the subject matter of the claims is novel and inventive. Applicant requests the restriction be withdrawn.

This is not found persuasive because of the reasons made of record mailed on 7/1/02 and further discussed below. First, the special technical feature of Group I is a conjugate comprising antennapedia homeodomain and a second region not naturally associated with the first region, wherein the first region is non-denatured. The special technical feature is not necessary the invention of each and every claim, but a technical feature that is shared by all the inventions. For example, claim 1 does not have the limitation of having a second region comprising more than 100 amino acids. As such, the argument of the Schutze-Redelmeier reference does not have more than 100 amino acids in second region is not valid. Similarly, claim 1 does not recite a

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purified conjugate wherein the purification process does not render the conjugate denatured. As such, the argument that the conjugate in the Schutze-Redelmeier reference is not in non-denaturing conditions after purification is not valid because the conjugate was not denatured before purification. Therefore, the special technical feature of Group I and shared by the rest of the Groups do not make a contribution over the prior art, and the unity of invention is lacking.

Second, 37 CFR 1.499 states that "if the examiner finds that a national stage application lacks unity of invention under rule 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner." Therefore, even the PCT application was determined to have unity of invention, this present restriction requirement is still proper.

This requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 10-14, 16, 17 and 24 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-9 and 19-23 are currently under examination on merits (claim 21 were inadvertently left out in the previous office action, and hereby included in Group I).

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in the current application. The priority date of 9/2/1997 is granted.

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Claim Objections

Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 20 is drawn to a conjugate comprising a first region of Ant homeodomain and a second region of a histone protein. Claim 7, the parent claim of claim 20, is drawn to a conjugate comprising a first region of Ant homeodomain and a second region of a DNA binding domain. Claim 20 does not further limit claim 7.

Claim 22 and 23 are objected to as being dependent upon a non-elected base claim (12). But for the purpose of examination, the limitations of claim 12 will be read into claim 22 and 23. Applicant is advised to rewrite the claim in independent form including all of the limitations of (non-elected) base claim (12).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 8, 9 and 21, the recitation of "wherein the second region comprises an NOI" renders the claims indefinite because the nature of invention is unclear. Claim 1, the parent claim of 8, 9 and 21, appears to be drawn to a chimeric protein conjugate comprising a homeodomain of antennapedia and a second protein of different origin. It is unclear if claims 8,

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9, 21 are drawn to a conjugate comprising a homeodomain of antennapedia with a nucleic acid of interest binds to the ant homeodomain, a chimeric protein as recited in claim with a nucleic acid binds to the second protein, or a ant homeodomain protein-DNA conjugate that is linked chemically. Appropriate clarification is suggested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Schutze-Redelmeier et al. (AR)

Claims 1, 3 and 19 are drawn to a protein conjugate or a fusion protein comprising a first region that is a homeodomain of antennapedia and a second region that is not associate with the first region, wherein the first region is not denatured. The claims are further drawn to said conjugate for use in a expression system.

Schutze-Redelmeier et al. disclose a fusion polypeptide comprising a homeodomain of antennapedia and a HLA-Cw3 CTL epitope, or an influenza nucleoprotein peptide (see page 651, Figure 1, and col. 1, 3rd paragraph). This conjugate is not denatured before the purification process. Therefore, Schutze-Redelmeier et al. disclose the instantly claimed invention.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schutze-Redelmeier et al., in view of Prochiantz. (AP)

The teaching of the Schutze-Redelmeier et al. is discussed above. However, Schutze-Redelmeier et al. does not teach that the conjugate is linked by disulfide bond.

Prochiantz teaches that the internalization of ant homeodomain conjugated polypeptide is not dependent on whether the polypeptide is at N-terminus or C-terminus of ant region. Prochiantz also teaches that in genetically or chemically produced chimeric peptides the cargo is C-terminally linked whereas it is N-terminally linked when the linkage is through a thiol (a disulfide bond).

It would have been obvious to one of ordinary skill of art to make a conjugate comprising an ant homeodomain and a second polypeptide that is linked by a disulfide bond because of the teaching of Schutze-Redelmeier et al., who teach a conjugate comprising a homeodomain of ant linked to a HLA-Cw3 CTL epitope or an influenza nucleoprotein peptide, and Prochiantz et al., who teach that ant can also deliver peptides linked to it by disulfide bond across the membrane. The ordinary artisan would have been motivated to do so link the protein that needs to be delivered on the N-terminal of ant homeodomain, as suggested by Prochiantz. The skill of art in crosslink peptide is considered to be high, and crosslink peptides by disulfide linkage is routine

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experimentation. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success to make a conjugate with ant homeodomain linked to a second peptide by disulfide bond. Therefore, the invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 4-7 are objected to for being dependent on a rejected claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
October 21, 2002



JAMES KETTER
PRIMARY EXAMINER